REMARKS

STATUS OF THE CLAIMS

Claims 8-15 were pending in this application. Claims 4-7 were previously withdrawn with the possibility of rejoinder; claims 4-7 are method claims dependent on the pending composition claim 8. Claims 9-10 and 14-15 are currently withdrawn as being drawn to a non-elected sequences with the possibility of rejoinder should generic claim 8 be found to be allowable.

Claims 4, 8, 9, 10, 11 and 14 have been amended herein.

Following entry of the amendments claims 8, 11, 12, and 13 will be pending and at issue.

SUPPORT FOR AMENDMENTS TO THE CLAIMS

The claims have been amended to replace the language "A composition comprising a first isolated polynucleotide and a second isolated polynucleotide ..." with the language "A set of polynucleotides comprising a first isolated polynucleotide and a second isolated polynucleotide ..." Support for the amendments can be found throughout the specification as filed, e.g., at paragraph [0016].

The claims have been amended to replace "a full-length complement" with "a complement" and to replace "the second polynucleotide" with "the second isolated polynucleotide." These amendments were made to merely correct informalities in the claim language.

The amendments to the claims therefore add no new matter and entry is respectfully requested.

SUPPORT FOR AMENDMENTS TO THE SPECIFICATION

The abstract of the disclosure was amended to merely correct an informality and delete the language "Described herein." No new matter is added and entry is respectfully requested.

OBJECTION TO THE SPECIFICATION

The abstract of the disclosure was objected to because "the abstract begins with "described herein. Correction is required."

Applicant has amended the abstract and withdrawal of the objection is requested.

REJECTIONS UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

Claims 8 and 11-13 were rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite.

The Examiner stated that "The metes and bounds of the claim with the recitation "full length complement is unclear …" Without agreeing with the Examiner's position but rather to further prosecution, Applicant has amended claims 8 and 11 to delete the language "full-length." The rejection is moot as drawn to the amended claims and Applicant requests withdrawal of this rejection.

The Examiner stated that "Claim 8 recites the limitation of "the second polynucleotide" … There is insufficient antecedent basis of this limitation in the claim. The claim recites a "second isolated polynucleotide …"" Applicant has amended claim 8 accordingly. The rejection is moot as drawn to the amended claims and Applicant requests withdrawal of this rejection.

REJECTIONS UNDER 35 U.S.C. § 112, FIRST PARAGRAPH

Claims 8 and 11-13 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. The Examiner stated that

> The newly amended claim(s) contain subject matter that changes the scope of the claim and is not supported in the specification and raises issues of new matter.
>
> **********
>
> Amended claim 8 with the recitation "the first isolated polynucleotide consists of SEQ ID:No. 4" and the recitation of "the second polynucleotides that consists of SEQ ID No. 8" changes the scope of the claim and a compositions consisting of SEQ ID No. 4 and 8 is not supported in the specification and raises the issue of new matter. The specification does not teach a composition that comprises two isolated polynucleotides that consists of SEQ ID No. 4 and 8. The originally filed claims recite a composition comprising "an" amplicons (see claim 1) and the specification teaches that nucleotide sequence are identified in SEQ ID No. 4,8,

> 12, 16, and 20 (see paragraph 6). However, the specification does not teach the amplicons that consist of SEQ ID No 4 and 8 in a composition together.

Applicant respectfully disagrees. Applicant notes that at paragraph [0016], the specification describes using PCR to determine the presence of SEQ ID NO:4 and SEQ ID NO:8, e.g., to PCR amplify the sequences resulting in two isolated polynucleotides. Without agreeing with the Examiner's position but rather to further prosecution, Applicant has amended the claims to recite "a set of polynucleotides" rather than "a composition."

The rejection is moot as drawn to the amended claims and Applicant requests withdrawal of this rejection.

REJECTIONS UNDER 35 U.S.C. § 103

Claims 8 and 11-13 were rejected under 35 U.S.C. 103(a) as allegedly unpatentable over Hu et al (1998) in view of GenBank Accession Number AF053947 and Hogan et al (US Patent 5541308). Applicant respectfully disagrees.

The Examiner stated that

> Hu et al. analysis of the pMTl virulence associated plasmid of Yersinia pestis. The plasmid, pMTl compromises nucleotides 85237-85136 which are identical to SEQ ID No. 4 and nucleotides 13354-13500, which are identical to SEQ ID No. 8 (alignment provided on 08/07/2006). Hu et al. teaches that SEQ ID No. 4 is part of the gene for murine toxin (see table 3).
>
> … Hu et al. does not teach a composition comprising a first isolated polynucleotides consisting of SEQ ID No. 4 and a second isolated polynucleotide consisting of SEQ ID No. 8. Hu et al. does not teach fragments of isolated polynucleotides that are 18-33 nucleotides in length nor does Hu et al. teach SEQ ID No. 1-3 and 5-7.
>
> … GenBank accession number AF053947 teaches the entire genomic sequence of plasmid, pMTl of Y. pestis. …
>
> … Hogan et al. teaches the use of specific primers and probes to amplify the 16s region of bacteria. … Though, Hogan et al. does not specifically teach the SEQ ID Nos 1-3 and 5- 7, he does suggest the fragmentation of a larger fragment (i.e. the GenBank Accession Number AF053947) into smaller oligonucleotide probes …
>
> Therefore, the ordinary artisan would have been motivated to select any number of oligonucleotide fragments from Accession Number AF05397 and the sequence

provided by Hu et al. to include SEQ ID Nos 1,2,3,5,6, and 7 which are fragments of SEQ ID No. 4 and 8 that are contained by Accession Number AF05397.

... Therefore the ordinary artisan would have been motivated to isolate and select any fragment within the pMTl plasmid to detect Y. pestis, including the amplicons of SEQ ID No. 4 and 8. ...

... It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to use an amplified sequence of Yersinia as taught by Hu et al, GenBank access No. AF05397 and design constraints of probes taught by Hogan et al. to obtain equivalent alternative probes, primers, and arnplicons of the claimed invention. The ordinary artisan would be motivated to have designed and test new probes to obtain additional oligonucleotides that function to detect Yersinia and identify oligonucleotides with improved properties.

Applicant's invention is a species that is not rendered obvious by the genus taught by the prior art

The Examiner is arguably describing a genus (any number of fragments of undefined length and sequence of the *Yersinia pestis* genome) to improperly render obvious the species that is Applicant's claimed invention, e.g., SEQ ID NO:4 and SEQ ID NO:8. In *In re Baird* the Federal Circuit stated that "The fact that a claimed compound may be encompassed by (prior) disclosed generic formula does not by itself render that compound obvious." In the instant case, the fact that SEQ ID NO:4 and SEQ ID NO:8 may be encompassed by a combination of art disclosing any number of fragments of undefined length and sequence of the *Yersinia pestis* genome does not by itself render SEQ ID NO:4 and SEQ ID NO:8 obvious.

The obviousness argument is rebutted using evidence that the claimed invention possesses unexpected properties.

In contrast to the properties of any fragment of undefined length and sequence from the *Yersinia pestis* genome, isolated polynucleotides consisting of SEQ ID NO:4 and SEQ ID NO:8 of the instant invention have the unexpected property of being useful for detection of *Yersinia pestis* in a sample without problems found in prior art methods, e.g., with no false positives and no false negatives.

Problems with prior methods for detection of *Yersinia pestis* in a sample were described in the specification:

> [00013] Existing detection methods have resulted in a higher than acceptable rate of false positive and false negative results. Such results are inadequate and can create confusion regarding the appropriate countermeasures, if any, that should be undertaken because it is unclear whether the bacterium is present or not. If the bacterium is not present, undertaking counter measures may cause undue expense and create unwarranted concern among those that may incorrectly believe they have been exposed.
>
> [00014] Although the genome for *Yersinia pestis* has already been mapped, this alone was not sufficient to develop a reliable and accurate detection mechanism because the current methods use nucleotide sequences that may be common to many different bacteria. Thus, existing detection methods could not distinguish between various bacteria, which resulted in higher than acceptable false positive detection rates. Similarly, some existing detection methods resulted in false negative results because they were not sensitive enough to detect the bacterium.

In addition, problems detecting *Yersinia pestis* have been described in the art. Reported problems include specificity, sensitivity, accurate detection of multiple *Yersinia pestis* strains that differ by the presence or absence of various plasmid elements, and speed. HIGGINS (Higgins et al (1998) J. Clin. Microbio. 36:2284, cited in Applicant's IDS) describes a 5' nuclease PCR to detect *Yersinia pesti;* HIGGINS reports false negatives and the failure of the assay to detect *Yersinia pestis* strains that do not include the target pla gene (page 2286, last paragraph). IQBAL (Iqbal et al (2000) Mol. And Cell. Probes 14:109, cited in Applicant's IDS) describes problems with both specificity and sensitivity in other reports (Discussion, page 112); IQBAL describes a TaqMan based assay that can detect only some strains of *Yersinia pestis* (Table 2, first 5 rows). RADNEDGE (Radnedge et al (2001) Appl. Environ. Microbio. 67:3759, cited in Applicant's IDS) describes a difficult process for identifying 4 pairs of PCR primers that do not yield false positives; only one of the four pairs, e.g., only one amplicon, successfully detects all tested *Yersinia pestis* strains (biovars) (Table 2 and last paragraph, page 3761).

In contrast to the problems described in the art, Applicant's claimed set of isolated polynucleotides consisting of SEQ ID NO:4 and SEQ ID NO:8 can be used for detection of

Yersinia pestis with no false negatives and no false positives. This is demonstrated in the Examples section of the specification. The described experiment showed that detection of *Yersinia pestis* DNA was successfully accomplished using detection of polynucleotides consisting of SEQ ID NO:4 and SEQ ID NO:8. In contrast, polynucleotides consisting of SEQ ID NO:4 and SEQ ID NO:8 could not be detected in environmental soil samples, demonstrating that false positives were not obtained using Applicant's invention.

In conclusion, polynucleotides consisting of SEQ ID NO:4 and SEQ ID NO:8 have the unexpected property of being useful for detection of *Yersinia pestis* with no false positives of false negatives. Therefore, a prima facie case of obviousness is not made. Withdrawal of this ground of rejection is respectfully requested.

STATEMENT OF SUBSTANCE OF INTERVIEW

Applicant thanks the Examiner for her time during a telephone interview on September 11, 2007. Examiner Bausch and Applicant's representative, Patent Agent Susan Hubl were present for the interview. No exhibits or demonstrations were presented or discussed. During the interview, claim 8 was discussed. Patent Agent Susan Hubl asked if changing the language from " a composition comprising" to " a set of polynucleotides" would overcome the new matter rejection. Examiner Bausch indicated that such an amendment might overcome the rejection.

CONCLUSION

Consideration of the claims is respectfully requested, and a notice of allowance is earnestly solicited. If the Examiner has any questions concerning this Response, the Examiner is invited to telephone Applicant's representative at (415) 875-2316.

Respectfully submitted,
MCCREADY ET AL

Dated: October 3, 2007 By: /Susan T. Hubl/

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